conditions of these patients were all maintained with placebo capsules for at least five to seven days during the withdrawal phase. While clear symptoms of withdrawal were observed, no severe reactions (eg, seizures or psychotic reactions) occurred. In keeping with our findings, few instances of severe withdrawal reactions associated with termination of *clinically accepted* doses of benzodiazepines have been reported in the literature. In the case reports cited by Drs Bargmann and Wolfe, the observations were made in uncontrolled conditions in which other factors may have been responsible for the reactions noted. In light of the widespread use of the benzodiazepine compounds, it is striking that so few instances of extreme withdrawal symptoms have been reported. However, more research, conducted under appropriately controlled conditions, is needed to evaluate this issue.

Drs Bargmann and Wolfe also raise questions about the efficacy of benzodiazepines in long-term use. Our recent report addresses this issue in only a preliminary manner. We are currently analyzing, for future publication, data from our study that support more directly the efficacy of long-term diazepam therapy.

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Risk Factors for Persistent Middle-Ear Effusions

To the Editor.—Kraemer et al[1] compared children with persistent middle-ear effusion (PMEE) admitted to a hospital for tympanostomy tube insertion with children admitted for other types of surgery and matched to patients with PMEE by age, sex, season, and surgical ward. Parents were interviewed about children's household exposure to cigarette smoke, frequency of nasal congestion, and frequency of defined atopic symptoms. The ratios of the proportions of children with PMEE to the proportions of children without PMEE in whom these factors were present were expressed as relative risks.

When relative risks were calculated individually for nasal congestion, cigarette smoke exposure (as measured by whether household residents reportedly smoked more than 0.5 packs per day), and atopy, nasal congestion was significantly different in children with and without PMEE, but cigarette smoke exposure and atopy were not. When risks were calculated for the three factors in pairs, exposure to cigarette smoke plus congestion and congestion plus atopy were significantly more frequently present in children with PMEE than in those without PMEE. Cigarette smoke exposure plus atopy could not be tested because of inadequate numbers of subjects. When all three factors were combined, the combination was significantly more frequent in children with PMEE than in those without PMEE.

Data derivable from the article's Table 2 show that when the influence of nasal congestion is controlled in the analysis of the influence of exposure to smoking on PMEE, the children exposed to smoking and those not exposed differed little in the proportion who had PMEE (Table).

Similar calculations show that, within the congestion and no-congestion groups, the proportions of atopic and nonatopic children who had PMEE were similar—74% and 68%, respectively, in those with congestion and 33% and 35%, respectively, in those without congestion.

Using other cutoff points and other measures of cigarette smoke exposure (Table 1), the authors found, in the small numbers of subjects with the highest levels of exposure, differences in relative risk between subjects with and without PMEE that were of borderline statistical significance, but they did not find a linear trend of increasing risk with increasing exposure.

The authors interpreted the analyses they reported as indicating that nasal congestion, cigarette smoke exposure, and atopy were all "important risk factors." We believe instead that the apparent associations between cigarette smoke exposure and PMEE, and between atopy and PMEE are probably artifactual and resulted (1) from combining, in the Table 2 analyses, cigarette smoke exposure and atopy each with nasal congestion, which *was* strongly associated with PMEE, and (2) from not having separated, in the Table 1 analyses, smoking from nasal congestion, or atopy from nasal congestion.

We do not believe that evidence presented by Kraemer et al establishes either cigarette smoke exposure or atopy as risk factors for PMEE.

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1. Kraemer MJ, Richardson MA, Weiss NS, et al: Risk factors for persistent middle-ear effusions: Otitis media, catarrh, cigarette smoke exposure, and atopy. *JAMA* 1983;249:1022-1025.

In Reply.—The letter by Rogers et al details their objections to our analysis of the risk factors for persistent middle ear effusions. They claim that because household cigarette smoke exposure and an atopic history seem to be strongly related to nasal congestion, which in turn is strongly related to PMEE, the apparent associations of PMEE with cigarette smoke exposures and atopy are only artifactual. They support their assertion by noting that, when the data from Table 2 are adjusted for the presence of nasal congestion, there is then no difference in the proportion of cases and controls who were atopic or exposed to cigarette smoke.

However, we believe that it is *inappropriate* to control for nasal congestion when assessing the risk for PMEE associated with exposures to household cigarette smoke and with atopy. This is because of our feeling that nasal congestion should not be considered as a confounder in this instance but rather as a means by which the adverse effect of atopy or smoke inhalation on the development of PMEE is mediated. If nasal congestion is not a determinant of household cigarette exposure or atopy but is actually a consequence of their actions, controlling for this variable will spuriously reduce the relative risk associated with cigarette smoke exposures and atopy by forcing cases and controls to be artificially similar with regard to these factors.[1]

Thus, we contend that our original analysis was correct and that the results of our study support the hypothesis of an etiologic role for atopy and cigarette smoke exposure in the development of PMEE.

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1. Greenland S, Neutra R: Control of confounding in the assessment of medical technology. *Int J Epidemiol* 1980;9:1-8.

Association Between Smoke Exposure, Nasal Congestion, and PMEEs*

	Nasal Congestion Present		Nasal Congestion Absent	
	PMEE (%)	Control (%)	PMEE (%)	Control (%)
Smoke exposure	24 (73)	9 (27)	14 (39)	22 (61)
No smoke exposure	21 (68)	10 (32)	17 (33)	35 (67)

*PMEE indicates persistent middle-ear effusion.

Source: https://www.industrydocuments.ucsf.edu/docs/zpnx0000

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